~~Confidential~~

Helsinki, 14 April 2021

Addressees
Registrant(s) of JS_122-20-3_TIPA as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
20/12/2019

Registered substance subject to this decision ("the Substance")
Substance name: 1,1',1''-nitrilotripropan-2-ol
EC number: 204-528-4
CAS number: 122-20-3

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***20 July 2022***.

Requested information must be generated using the Substance unless otherwise specified.

A. Information required from all the Registrants subject to Annex IX of REACH

1. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

2. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

Reasons for the request(s) are explained in the appendix entitled "Reasons to request information required under Annexes IX of REACH".

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII to X to REACH, for registration at [redacted]

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix A: Reasons to request information required under Annex IX of REACH

1. Long-term toxicity testing on aquatic invertebrates

Long-term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

You have provided a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification:

"In Annex IX of Regulation (EC) No 1907/2006, it is noted that long-term toxicity to aquatic invertebrates shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on aquatic invertebrates. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or CLP-Regulation (EC) No 1272/2008 is assessed to be a PBT or vPvB. However, the presented hazard assessment of triisopropanolamine based on available data (companies studies, comprehensive literature search) reveals neither a need to classify the substance as dangerous to the environment, nor as a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Moreover, the risk characterization shows that the RCRs for the aquatic environment is clearly <1, indicating no need for further information and testing".

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to aquatic invertebrates under Column 1. It must be understood as a trigger for providing further information on aquatic invertebrates if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Therefore, your adaptation is rejected.

In your comment to the draft decision, you propose to adapt the information requirements in accordance with Annex XI, Section 1.3, i.e. by applying a QSAR approach.

You have used the OECD QSAR Toolbox v4.4. to select 8 analogue substances for which experimental values for 21-d NOEC for reproduction on *Daphnia magna* are available. You have then used a linear regression to model the log-transformed NOEC values (as molar concentrations) of those 8 analogue substances as a function of their corresponding log Kow values. From that model you have predicted a 21-d NOEC of 27.5 mg/L for the Substance using a log Kow value of -0.015 as input value to the model.

We have assessed this information and identified the following issue:

Annex XI, Section 1.3. specifies that the following conditions must be fulfilled whenever a (Q)SAR approach is used:

1. the prediction needs to be derived from a scientifically valid model,
2. the substance must fall within the applicability domain of the model,
3. results need to be adequate for the purpose of risk assessment or classification and labelling, and
4. adequate and reliable documentation of the method must be provided.

With regard to these conditions, we have identified the following issue(s):

Under ECHA Guidance R.6.1.3.4 a prediction is adequate for the purpose of classification and labelling and/or risk assessment when the model is applicable to the chemical of interest with the necessary level of reliability.

The model you have proposed predicts a 21-d NOEC of 27.5 mg/L for the Substance but with an associated 95% prediction interval ranging from 0.11 to 6.88E+03 mg/L, as reported in your comments.

In addition, based on the information provided in your comments to the draft decision, it is possible to calculate the tolerance interval for your prediction. The uncertainties of a model prediction are due in part to the limited size of the training set (the sampling error) but also to the intrinsic variability of the data. Both aspects can be quantified with a tolerance interval. The lower bound of the 95% tolerance interval (1-sided, significance level: 5%) calculated for the 21-d NOEC predicted by your model for a log Kow of -0.015 is 0.11 mg/L. More specifically, it can be calculated from your model that the probability that the 21-d NOEC is below 1 mg/L for a substance with a log Kow of -0.015 is 29.51% with 95% confidence. Similarly, the probability (with 95% confidence) that the 21-d NOEC is below 0.1 mg/L can be calculated as 11.22% and the probability (with 95% confidence) that the 21-d NOEC is below 0.01 mg/L as 3.26%.

Therefore, the predicted 21-d NOEC value of 27.5 mg/L is highly uncertain. This value is as such not reliable for assessing the long-term toxicity of the Substance to aquatic invertebrates and not adequate for the purpose of classification and labelling and/or risk assessment.

On this basis, the information requirement is not fulfilled.

2. Long-term toxicity testing on fish

Long-term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

You have provided a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification:
"*In Annex IX of Regulation (EC) No 1907/2006, it is noted that long-term toxicity to fish shall be proposed by the registrant if the chemical safety assessment indicates the need to investigate further the effects on fish. According to Annex I of this regulation, the chemical safety assessment triggers further action when the substance or the preparation meets the criteria for classification as dangerous according to Directive 67/548/EEC or Directive 1999/45/EC or CLP-Regulation (EC) No 1272/2008 is assessed to be a PBT or vPvB. However, the presented hazard assessment of Triisopropanolamine based on all kind of available data (companies studies, comprehensive literature search) reveals neither a need to classify the substance as dangerous to the environment, nor as a PBT or vPvB substance, nor are there any further indications that the substance may be hazardous to the environment. Moreover, the risk characterization shows that the RCRs for the aquatic environment is clearly <1, indicating no need for further information and testing. Therefore, and for reasons of animal welfare, a long-term toxicity in fish is not provided*".

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Animal welfare does not constitute as such a valid justification to omit the standard information requirements of Annexes VII – X or a valid adaptation to these information requirements.

Your adaptation is therefore rejected.

In your comments to the draft decision, you acknowledge the rejection of the adaptation of the information requirement based on the Decision of the Board of Appeal in case A-011-2018. However, you indicate that you do not intend to perform a long-term toxicity to fish, but to use a weight of evidence approach as a new adaptation for this information requirement. In support of this weight of evidence approach, you have provided the following justifications:

a) The Substance is fully characterised and is not persistent;
b) No structural alert for protein binding was found which is deemed to be an indication of the absence of elevated toxicity;
c) Fish is not the most sensitive trophic level in the available short-term toxicity test results for the Substance;
d) Long-term toxicity to fish could be extrapolated from short-term toxicity to fish using an acute-to-chronic ratio (ACR) of 100;
e) Long-term toxicity testing on fish is not necessary for the PBT assessment of the Substance;
f) Unnecessary animal testing should be avoided.

ECHA has assessed this information.

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

According to ECHA Guidance R.4.4, a weight of evidence adaptation involves an assessment of the relative values/weights of different pieces of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance of the information for the given regulatory information requirement. Subsequently, relevance, reliability, consistency and results of these pieces of information must be balanced in order to decide whether they together provide sufficient weight to conclude that the Substance has or has not the properties investigated by the required study.

To fulfil the information requirement, normally a study performed according to OECD TG 210 must be provided. OECD TG 210 requires the study to investigate parameters related to the survival and development of fish in early life stages from the stage of fertilized egg until the juvenile life-stage following exposure to the test substance are measured, including:

1) the stage of embryonic development at the start of the test, and
2) hatching of fertilized eggs and survival of embryos, larvae and juvenile fish, and
3) the appearance and behaviour of larvae and juvenile fish, and
4) the weight and length of fish at the end of the test.

None of the pieces of information provided address these key investigations.

ECHA notes in particular that:

a) Even though the Substance is not persistent, environmental exposure still occurs as shown by your chemical safety assessment.
b) Toxic effects are not restricted to protein binding, toxicity can be triggered by other

mechanisms.

c) For registrations at more than 100 tpa, REACH does not foresee that information on long-term toxicity to fish could be extrapolated from information on short-term toxicity or from information on other trophic levels.
d) Regarding the ACR approach, REACH does not foresee that information on long-term aquatic toxicity could be extrapolated from information on short-term aquatic toxicity. In any case, the ACR approach is not substance-specific. You indicate that an ACR of 100 would cover at least 90% of all organic chemicals. However, this does not constitute a proof that a higher ACR value does not apply to the Substance.
e) Long-term toxicity testing on fish is not necessary for the PBT assessment of the Substance but is a standard information requirement of Annex XI Section 9.1.6.
f) As explained above, animal welfare does not constitute as such a valid justification to omit the information requirement or a valid adaptation to this information requirement.

Taken together, those pieces of information do not provide information on long-term toxicity of the Substance on fish and, therefore, they cannot contribute to the conclusion on the key investigation for this information requirement. Accordingly, it is not possible to conclude, based on any piece of information alone or considered together, whether the Substance has or has not the properties foreseen to be investigated in an OECD TG 210 study.

On this basis, the information requirement is not fulfilled.

Appendix B: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

1. Under Article 13(3) of REACH, all new data generated as a result of this decision must be conducted according to the test methods laid down in a European Commission Regulation or to international test methods recognised by the Commission or ECHA as being appropriate.

2. Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses must be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[2].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[3].

[2] https://echa.europa.eu/practical-guides
[3] https://echa.europa.eu/manuals

Appendix C: Procedure

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

ECHA followed the procedure detailed in Articles 50 and 51 of REACH.

The compliance check was initiated on 26 February 2020.

ECHA notified you of the draft decision and invited you to provide comments.

ECHA took into account your comments and did not amend the request(s).

ECHA notified the draft decision to the competent authorities of the Member States for proposals for amendment.

As no amendments were proposed, ECHA took the decision according to Article 51(3) of the REACH Regulation.

Appendix D: List of references - ECHA Guidance[4] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[5]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[5]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[6]

[4] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[5] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[6] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix E: Addressees of this decision and their corresponding information requirements

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.